EXHIBIT C

Pacific Biosciences of California (PACB) Q4 2020 Earnings Call Transcript

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PACB earnings call for the period ending December 31, 2020.

Pacific Biosciences of California (PACB -2.71%)
Q4 2020 Earnings Call
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Contents:

The Motley Fool Transcripts

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Prepared Remarks:

Operator

Thank you for standing by, and welcome to the Pacific Biosciences of California, Inc. fourth-quarter 2020 earnings conference call. [Operator instructions] I would now like to hand the conference over to Trevin Rard. Please go ahead.

Trevin Rard -- *Investor Relations*

Thank you. Good afternoon, and welcome to the Pacific Biosciences fourth-quarter 2020 earnings conference call. We hope that you're keeping well during this time. Earlier today, we issued a press release outlining the financial results we'll be discussing on today's call, a copy of which is available on the Investors section of our website at www.pacb.com or, alternatively, as furnished on Form 8-K available on the Securities and Exchange Commission website at www.sec.gov.

With me today are Christian Henry, president and chief executive officer; Susan Kim, chief financial officer; Mark Van Oene, chief operating officer; and Ben Gong, vice president of finance. Similar to last quarter, we are hosting our conference call from a number of different locations, so please bear with us if there are any technical issues or pauses. Before we begin, I'd like to remind you that on today's call, we may be making forward-looking statements, including plans and expectations relating to our financial projections; plans and expectations relating to our research and development efforts; plans and expectations, including expectations with respect to timing, sales and revenue projections; plans in connection with our collaboration partners, including expectations regarding sales related to our collaboration with Invitae; plans and expectations to grow, accelerate and expand our product portfolio, commercial efforts and commercial footprint, including plans related to our products to increase throughput, lower cost and develop workflows; adoption of our sequencing technology as a transformative and fundamental tool in research, clinical and genetic testing applications; the use of our technology for specific projects and applications, including in connection with

epigenetic COVID-19, cancer and rare disease clinical research applications; potential growth and impact of growing our commercial team and research and development teams; plans to make COVID-19 protocols widely available to commercial laboratories; the need for more expansive and robust viral surveillance strategies due to the emergence of more infectious COVID-19 mutations; and other future events, such as the impact of COVID-19 pandemic on our business partners, our business partners, customers and employees and the use and advantage of our products in COVID-19 research. You should not place undue reliance on forward-looking statements because they are subject to assumptions, risks, and uncertainties and may differ materially from actual results.

In particular, the extent of COVID-19's continued impact on our business will depend on several factors, including the severity, duration, and extent of the pandemic, as well as actions taken by government, businesses, and consumers in response to the pandemic, all of which continue to evolve and remain uncertain at this time. These risks and uncertainties are more fully described in our Securities and Exchange Commission filings, including our most recently filed reports on Forms 8-K, 10-K, and Form 10-Q. Pacific Biosciences undertakes no obligation to update forward-looking statements. In addition, please note that today's call is being recorded and will be available for audio replay on our Investors section and our website shortly after the call.

Investors electing to use the audio replay are cautioned that forward-looking statements made on today's call may differ or change materially after the completion of the live call. I'd now like to turn the call over to Christian.

Christian Henry -- *President and Chief Executive Officer*

Thank you, Trevin. And good afternoon, and thank you for joining us today. Before we begin, I'd like to everyone know that Ben Gong, our vice president of finance, is retiring this quarter. As a result, this is his last earnings call.

On behalf of all the employees at PacBio, Susan and I would like to thank him for his significant contributions to the company over the past decade. Before the market opened this morning, we announced that SoftBank is making an investment of $900 million in the company to support the acceleration of our growth initiatives. We are excited to partner with SoftBank as they can help us expand our reach on a global scale. We believe that this investment validates our leadership position in long-read sequencing and will help enable us to accelerate the expansion of our product portfolio, expand our commercial footprint, and ultimately, to realize our vision that whole-genome sequencing using our technology will become a fundamental tool for the use in a broad range of both research and clinical applications.

On our last earnings call, I described some of our key priorities, and I am pleased to report that we're making progress on a number of fronts, including our ability to execute and grow the business. For my prepared remarks, I will briefly review our Q4 financial highlights and then describe key business highlights and summarize our expansion efforts including the addition of several key management hires. Susan will then walk us through the detailed financials for the fourth quarter and provide some thoughts around our outlook for 2021. So starting with an overview of our Q4 2020 financial results.

Total revenue for the quarter was $27.1 million, up 41% sequentially from Q3 of 2020. We exceeded our internal Q4 target for revenue, and we did not see a significant negative impact from the COVID-19 pandemic during the quarter. Instrument revenue was $13.6 million, up 76% compared to Q3 of 2020. Our newly launched Sequel IIe was well received by our customers, which drove an increase in orders.

Additionally, we received several multi-system orders from customers like the Wellcome Sanger Institute and Berry Genomics. We delivered and installed 35 new Sequel II and IIe systems during the fourth quarter and ended the year with an install base of 203 Sequel II and IIe systems. Consumable revenue for the quarter was $10 million, up 25% sequentially from Q3 2020. System utilization on the Sequel II platform was higher in Q4 2020 than pre-COVID levels.

Annualized pull-through on the Sequel II install base in Q4 exceeded $180,000 per system compared with approximately $160,000 in Q3. We are pleased to see this increase in pull-through. However, we note that Q4 consumable revenue benefited from some seasonal stocking orders as is typical in the fourth quarter of the year. Susan will provide more details on our financial metrics later in the call.

Now, I'd like to provide a few updates and comments regarding the impact of the COVID-19 pandemic on our business. Going into Q4, we were cautious about the potential impact that the resurgence in infection rates in Europe and the United States would have on our sales for the quarter. Fortunately, just about all of our existing customers were operating throughout the quarter. And as I said before, average utilization on Sequel II systems was higher in Q4 than it was prior to the pandemic.

It should be noted that travel limitations did prevent us from installing some systems during the quarter, but the strength of the Sequel IIe orders enabled us to overcome these challenges. Looking forward, we believe that the pandemic will continue to cause some uncertainty in our revenue outlook as shutdowns could impact our ability to install new systems, and we believe that some customers may remain conservative with respect to capital spend. Additionally, on the topic of COVID, the emergence of the more infectious mutations in the U.K., South Africa, and elsewhere, over the last few months, has reinforced the need for more expansive and robust viral surveillance strategies. Governments and public health organizations around the world are moving quickly to identify and track the different COVID strains in their communities.

Notably, in the United States, the CDC contracted with LabCorp in early January to support the scale-up of COVID sequencing using PacBio HiFi technology. The COVID-19 whole-genome HiFi sequencing assay was developed as a research collaboration between scientists at the CDC, LabCorp, and PacBio beginning in early 2020. Already this year, LabCorp has purchased several additional Sequel II systems to ramp up their surveillance testing with HiFi COVID sequencing, and we look forward to working with LabCorp to continue to scale their operations to service this global need. It's exciting to see that their efforts are already making an impact as LabCorp was the first to identify the New South Africa variant in South Carolina and Virginia just last week.

We're pleased to announce that PacBio will now be making this high-throughput protocol widely available to commercial laboratories, academic researchers, and public health institutions globally, who wish to stand up robust high-throughput surveillance programs locally. We believe use of PacBio's highly accurate long-read, HiFi sequencing chemistry for COVID surveillance offers distinct advantages over other technologies, including fewer amplicon dropouts, easier amplicon balancing, and the ability to phase COVID genomes, which can detect the different strains infecting a given individual. We are proud to have contributed to the assay development that LabCorp and the CDC are now using to understand and get ahead of this rapidly mutating virus. We plan to build on this experience to further bring the benefits of our technology to bear in the fight against COVID.

Shifting gears to population-scale projects, as a result of the pandemic, some delays persist in the ramp-up of certain large sequencing projects, such as the All of Us human genome sequencing project in the United States, and to a lesser extent, the Darwin Tree of Life plant and animal sequencing project in the United Kingdom. However, the Wellcome Sanger Institute, where the Darwin Tree of Life samples are going to be sequenced, has started to prepare its facility to generate 2,000 high-quality reference genomes over the next two years. In anticipation of receiving those samples, the Wellcome Sanger Institute ordered seven new Sequel IIe systems this past quarter. Some of those systems were installed last quarter, and we expect the balance to be installed in the first half of this year.

Moving on to other business highlights. I'd like to discuss our collaboration with Invitae that we announced last month. PacBio and Invitae share a vision that whole-genome sequencing using PacBio HiFi read in a routine clinical setting, has the potential to fundamentally transform the genetic testing industry. Together, we are partnering to bring this vision to reality.

Currently, Invitae processes hundreds of thousands of samples per year. We believe that there is a significant opportunity to move the majority of those samples to whole-genome sequencing, which is why we are working with Invitae to develop a new ultra-high throughput sequencer and workflow that is expected to be capable of

operating at production scale. Under the agreement, Invitae will fund the development cost, as well as provide input on scaled clinical workflows. The new system is expected to enable Invitae to sequence up to hundreds of thousands of samples every year in a medium-sized production facility.

Upon completion of the new sequencer, PacBio will make the new system and associated consumables available to Invitae at preferential pricing for a defined period of time. In addition, PacBio will have the ability to commercialize the new sequencer to other customers as well. Given the expected scale of the new system, we would expect labs involved with running production scale whole genome projects to be candidates for placement of the new system. Developing an ultra-high throughput sequencer is an important step in our strategy to move toward a broad portfolio of systems and capabilities that allow our customers to choose the right system for their needs and for their budget.

The collaboration with Invitae is expected to run for five years. Over the first few years, we plan to develop the new sequencing platform and related workflows. We expect to rapidly hire more than 50 new people into our R&D organization, which will dramatically increase our R&D expense. While Invitae will be reimbursing us for these additional expenses, those reimbursement dollars may not be accounted for as an offset to these expenses.

Susan will describe the accounting for the collaboration in more detail later in this call. As far as revenue is concerned, we do not expect any revenue contribution stemming from the direct collaboration for the next few years. However, once the new system is commercially available, we expect to see a very significant increase in revenue, led by sales to Invitae. And before I get to organizational updates, I'd like to share some customer highlights that really demonstrate the power and the potential of PacBio HiFi sequencing technology.

First, we'd like to congratulate Dr. Dennis Lo and colleagues at the Chinese University of Hong Kong on the development of a new method for highly accurate simultaneous determination of DNA sequence and CPG methylation in one go, published in the PNAS Journal in January. This new method will help researchers explore the impact of epigenetic changes in humans and other organisms and has great potential in clinical research and eventually diagnostics in cancer and other disease areas where methylation changes are known to be important disease markers. We'd also like to congratulate the team at HudsonAlpha Institute of Biology for their work in leveraging PacBio HiFi read to help diagnose children with rare disease, who still are lacking an answer after short-read sequencing.

Their recent paper published in Human Genetics and Genomics Advances demonstrates the power of HiFi sequencing to capture more of the variation across the genome, which gives investigators and clinicians more information to make a diagnosis, saving precious time and resources and reducing the diagnostic odyssey. Shifting now to our organizational team. We are thrilled to have Mark Van Oene on board as our new chief operating officer. Mark has deep experience in genomics and brings a strong voice of customer into our R&D and operations organization.

In addition, Mark will be responsible for leading our corporate development activities, which will become increasingly important as we expand. We are also excited to have Peter Fromen on board as our chief commercial officer. Peter has been at the forefront of population-scale sequencing initiatives around the world and his vision and ability to execute will move our commercial organization to new levels. In addition to Mark and Peter, we have also recently hired four additional commercial executives, who will lead critical areas in product and strategic marketing, as well as commercial operations.

As I've indicated on our last call, the key strategy for the company is to increase our direct sales force globally. We're making great progress in this area as we've hired over 10 new quota-carrying sales personnel over the past few months, which puts us well on our way toward more than doubling our sales force. We expect our new sales reps to come up to speed over the first few quarters after they come on board and then become part of the engine that drives consistent revenue growth. To summarize, I am very encouraged by our performance in the fourth quarter.

For the second consecutive quarter, we met or exceeded our internal revenue targets. We have kick-started the new year with what promises to be a transformational collaboration with Invitae, and we have made significant progress in expanding our team to drive future growth. With that, I'll turn the call over to Susan, who will provide more details on our Q4 financial results and our current outlook for the first quarter. Susan?

Susan Kim -- *Chief Financial Officer*

Thank you, Christian, and good afternoon, everyone. Despite Q4 still being impacted by COVID-19 headwinds, the PacBio team delivered a very solid quarter that included sequential growth in bookings, revenues, and gross margins. As Christian mentioned, the Sequel IIe launch was stronger than anticipated, which resulted in orders in the fourth quarter, exceeding our internal expectations, including a number of multi-instrument orders from key customers. Total fourth-quarter revenue was $27.1 million, an increase of 42% from $19.1 million in Q3 of 2020 but a decrease of 3% from $27.9 million in Q4 of 2019.

The revenue breakdown was as follows: instrument revenue recognized in Q4 was $13.6 million, an increase of 76% from $7.7 million recognized in Q3 and down from $15.3 million recognized in Q4 of 2019. We installed 35 Sequel II and IIe systems during the fourth quarter, growing the install base of Sequel II and IIe Systems to 203 as of December 31. As the consumables are the same and customer usage patterns are expected to be similar across the Sequel IIe and IIe systems, we will continue to report a combined install base going forward. Consumable revenue for the fourth quarter of 2020 was $10 million, up 25% sequentially from $8 million sold in Q3 of 2020, and up 8% from $9.3 million sold in Q4 of 2019.

The sequential growth in consumable revenue reflects increased utilization on our growing install base of Sequel IIe and IIe systems, as well as the usual end of year stocking of consumables inventory. Since the start of the COVID-19 pandemic that resulted in our customer labs being shut down, we have since continued to see meaningful increase in our Sequel I and Sequel IIe utilization such that we have recently crossed a cumulative five petabases sequenced on our install base of Sequel II systems. Sequel II consumables represented approximately 78% of our total shipments in the fourth quarter, and roughly 20% of our consumable shipments were purchased for the older Sequel systems, and the remaining for the RS II systems. We expect the proportion of consumable sales from Sequel II systems to continue to grow as the install base of these systems continues to expand.

Service and other revenue was $3.5 million in Q4 2020, compared to $3.3 million in Q3 and $3.3 million in Q4 2019. Our service revenue has remained relatively flat over the past year as increased service on Sequel II systems has been offset by declines in service on RS II and Sequel systems. Moving on to gross profit and gross margin. In Q4 of 2020, we generated a gross profit of $11.4 million, representing a gross margin of 42% compared to a gross profit of $7.1 million, representing a gross margin of 37% in Q3 of 2020.

There are three key reasons why gross margin improved sequentially: first, ASPs on insurance sales were higher; second, we had improved product mix over Q3; and finally, higher volume in manufacturing improved factory utilization. Year over year, our gross profit and gross margin in the quarter declined from $12.9 million and 46% generated in Q4 of 2019 as a result of lower revenue and factory utilization, partially offset by higher ASPs on instrument sales. Moving on to operating expenses. Operating expenses in the fourth quarter of 2020 totaled $35.4 million, up 13% compared with $31.2 million in Q3 of 2020, and up 15% compared with $30.8 million in Q4 of 2019.

The increase in operating expense compared to the previous quarter and last year was a result of increased R&D expense related to new product development and an increase in SG&A expense as a result of the growth in our commercial team and the addition of several new executives and higher non-cash stock-based compensation expense. Noncash stock-based compensation expense included in operating expenses was $4.8 million in Q4 of 2020, up from $4.3 million in Q3 of 2020, and up from $3.4 million in Q4 of 2019. Net income in Q4 2020 was $74.9 million and net income per share on a fully diluted basis was $0.37 compared to a net loss of $23.7 million and net loss per share of $0.14 in Q3 2020, and a net loss of $100,000, which rounds to a net loss per share of $0 in Q4 2019. The large increase in income was primarily related to the $98 million one-time gain we recorded, which was associated with the reverse termination fee we received from Illumina back in January of last year and recognized in Q4 of 2020.

Turning to our balance sheet. We ended the fourth quarter with a balance of $318.8 million in unrestricted cash and investments compared with $208.6 million at the end of the third quarter of 2020. The increase in cash and investments was primarily a function of our follow-on offering in November that netted proceeds of approximately $94 million plus approximately $32 million in proceeds associated with employee stock option exercises, partially offset by approximately $16 million of cash used for operations. Inventory balances decreased in Q4 2020 to $14.2 million, representing a 4.2 inventory turns compared with $15.9 million at the end of Q3 2020, which represented 2.9 inventory turns due to the ramp in customer installations in Q4.

Accounts receivable increased in Q4 to $16.8 million, reflecting a DSO of 49 days compared with $11.8 million at the end of Q3 2020, reflecting a DSO of 56 days. As we look out into 2021, the impact of the pandemic on our revenue growth is still somewhat uncertain. However, with that said, I would like to provide a framework on how we see revenue growing during the year. We believe that revenue will grow significantly in the second half of the year as we start to realize the benefit of our expanded commercial investment and infrastructure.

In the short term, we expect Q1 revenues to be slightly lower than Q4 levels. While we expect the strength we saw in instrument sales last quarter to carry over into this quarter, we also foresee some softening in consumables sales in APAC, largely due to the Lunar New Year holiday. This is consistent with the seasonal revenue pattern we have seen over the past several years. Although we anticipate slightly lower revenue in Q1, we do anticipate gross margin will improve slightly compared to Q4 as our factory utilization continues to improve.

For Q1, we estimate noncash stock-based compensation expense will increase materially to between $10 million to $11 million, up from $4.8 million in Q4 due to new higher employee equity grants accounted for in our operating expenses. We are forecasting our total Q1 operating expenses to grow and to be in the mid- to

high $40 million. I would like to take a moment to provide additional context regarding the investments we intend to make in 2021. We plan to make significant investments in our business as we push forward with our key objectives.

Our first objective, expanding our commercial reach, includes a significant expansion of our commercial organization. We ended the year with 22 quota-carrying sales representatives, and we are targeting to more than double that number by the end of the year. Our second objective, driving the product development pipeline, will entail the development of multiple new products simultaneously. We ended the year with 158 people in our research and development organization, and we are targeting to hire more than 50 additional people in R&D this year.

Our third objective, market leadership in whole-genome clinical sequencing, is off to an accelerated start with our collaboration with Invitae. As Christian mentioned earlier, we are working with Invitae to develop an ultra-high throughput system and workflow designed to enable Invitae to sequence hundreds of thousands of samples per year. For the year 2021 alone, we are targeting to spend $20 million to $25 million on this project. While we expect Invitae to fund this project, we will likely recognize all or a substantial amount of this expense in the R&D expense line of our income statement in the period in which it has occurred.

The funding we received from Invitae is likely to be recorded as a liability on our balance sheet and may be amortized into revenue in later periods as we sell the developed products to Invitae in accordance with our agreement or released when other performance obligations are delivered or contingencies lapse. Please be advised that we are still analyzing the proper accounting treatment for these activities, and we do not expect to finalize how it will appear on our financial statements until we report our first-quarter 2021 results. Lastly, as we announced earlier today, we are thrilled to welcome SoftBank as a new long-term investor. The $900 million convertible note will provide the financial foundation for us to capitalize on the significant growth opportunities ahead.

The transaction is scheduled to close next week. As a result of this financing, $52 million of expense will be recognized on our P&L in Q1 to account for the expected repayment of the continuation advances due to Illumina as a result of the merger termination. In summary, we ended the year with nearly $319 million of cash on our balance sheet, and now, with the significant investment by SoftBank, that is expected to close next week, we will have well over $1 billion in capital, giving us a strong foundation to drive growth over the long term. With that, I will turn the call back to Christian.

Christian?

Christian Henry -- *President and Chief Executive Officer*

Thank you, Susan. To wrap up our prepared remarks, I'd like to reiterate our three core objectives for '21. First, we plan to dramatically expand our commercial footprint, so that we can serve more customers around the globe. Secondly, we plan to accelerate our product development pipeline with a focus toward increasing throughput, lowering costs, developing end-to-end workflows; and finally, developing a multi-product portfolio so that customers have access to the right long read sequencer for their scale and applications.

And thirdly, we're focused on moving our smart technology deeper into the clinical diagnostic market, where we believe we have unique advantages over other sequencing technologies. This will be done through the execution of high-quality partnerships such as the one with Invitae that we announced in January. My opening remarks touched on a number of specific accomplishments the team made toward executing on these strategies. Moving forward, we expect to increase our engagement in the global fight against COVID as we believe that HiFi reads can make a significant positive impact.

You'll see us work to expand our global network of collaborators in rare and inherited diseases, who seek to leverage pack by HiFi reads to solve 50% of the cases that elude diagnoses with other technologies today. In closing, we have a strong finish to a challenging 2020, and although headwinds associated with the pandemic still exist, I believe our core strategies, expanded leadership team, and improved execution will drive growth in 2021 and beyond. And finally, SoftBank's investment of $900 million provides us with the financial resources to work toward achieving our objectives. I believe we have a significant opportunity in front of us, and I'm excited about our future.

That concludes our prepared remarks, and with that, we'd like to now open it up for some Q&A.

Questions & Answers:

Operator

[Operator instructions] Your first question comes from Doug Schenkel with Cowen. Your line is now open.

Doug Schenkel -- *Chief Financial Officer*

Hey, good afternoon, everyone, and thank you for taking my questions. First off, thanks, Ben, for all your help over the years, and good luck on the next chapter. Christian, I want to just talk about kind of, I guess, a high-level strategic question. Illumina in attempting to acquire Pacific Biosciences was essentially attempting to go from being just a short-read sequencing company to be in both short and long read.

It's been asserted that PacBio could almost reverse that playbook, essentially going from being the dominant long-read sequencing company to be in both long read and short read. With that in mind, how are you thinking about the best way to achieve that? Is it organic or is it inorganic? And part of the reason I start with this question is, with the investment from SoftBank, does it change how you think about that question of organic versus inorganic?

Christian Henry -- *President and Chief Executive Officer*

Well, Doug, first of all, it's good to hear from you, and thank you for the question. When you think about this question, I'm going to first start and address what does the SoftBank capital do for us. There's no question that it gives us a lot more flexibility to think about how we can create scale, how we can create a multiproduct portfolio, and how we could drive our business forward faster. And I think one of the things I'm very interested in is a combination of organic and inorganic opportunities.

And I think the inorganic opportunities are more accessible to us, of course, now that we have some more capital to work with. With respect to the specific strategy of short read, long read, long read, short read, I think if you step up a higher level and try to think about what we can be as a company, we want to be the most advanced biological solutions company with a number of different products in our portfolio, and that could encompass obviously, long reads, where we're going with that in our leadership position and driving the accelerated development of products there. It could encompass short reads, there's obviously large markets that are uniquely accessible to short reads at least today. But it also could encompass market adjacencies, complementary technologies, abilities for us to look at the front end of our workflows, as well as the back end.

So developing those complete solutions for our customers. And I think right now, we're just so thrilled to have this relationship building with SoftBank to give us the capital we need to think big because I do think with our leadership team and our long read HiFi sequencing capability, we have a lot of opportunity in front of us.

Doug Schenkel -- *Chief Financial Officer*

That's super helpful. Thanks for that, Christian. And then maybe if I could just ask a second question on another recent development. You shared some additional details on the agreement with Invitae, which, of course, was a really exciting development over the last several weeks.

Regarding the five-year duration that you outlined, I just want to clarify, does that mean that this is an exclusive with Invitae over this period? And does that mean that's the expectation in terms of when there would actually be an instrument commercialized? I just want to maybe unpack a little bit about what happens during those five years and what comes after. And you also talked about the concept of essentially being able to have an industrialized PacBio instrument that would be well suited for larger central labs like Invitae, but not limited to Invitae. Is there a scenario where this agreement also leads to the development of instruments that are more well suited for clinical applications in a more decentralized approach? Thank you.

Christian Henry -- *President and Chief Executive Officer*

Yes. There's a lot to unpack there, Doug, but let me see how I can do. First, the agreement with Invitae is not an exclusive arrangement for any period of time, but rather, we are developing -- we're embarking on a long-term collaboration with them to develop multiple products. So the first product is much, much closer than five years out.

And that product will be this ultra-high-throughput sequencer that will give Invitae the power to do whole genome sequencing at production scale at prices substantially below $1,000. I believe, I said that in the press release in January. What the unique feature is, of course, is that we will be giving Invitae preferential pricing, but we will also be free to market that product and that sequence broadly to a number of different customers. And as you could imagine, we will leverage that technology to develop potentially offshoots of that product for more decentralized situations or different levels of throughput or capability, so that we can meet the needs of the market.

I think this is one of the core strategies that I've been talking about since I joined the company was developing a product portfolio that reaches each customer in the way they want to be -- in the way they want to do sequencing. And it does start at the high end with Invitae. But you can imagine that the technology will be applicable across a broad spectrum of customer types and applications. And so that's where we'll go from there.

We will have products beyond this first product with Invitae, but those will impact themselves over time, of

course. So hopefully, that helps a little bit for you, Doug?

Doug Schenkel -- *Chief Financial Officer*

Yes. Nicely done, Christian. That's sort of a lot, so thanks for all that color. I'll get back in the queue.

Christian Henry -- *President and Chief Executive Officer*

Great. Thank you, Doug.

Operator

Your next question comes from Tejas Savant from Morgan Stanley. Your line is open.

Tejas Savant -- *Morgan Stanley -- Analyst*

Hey, guys. Thanks for the timing this evening. Christian, can you share a little bit more color on sort of your early popsy conversations here? For the existing projects, you're participating in, including all of us in Darwin Tree of Life. How should we think about sort of the consumable pull-through on the Sequel in 2021 and beyond?

Christian Henry -- *President and Chief Executive Officer*

Yes. Thank you for the question. My expectation is that as these projects ramp, they would be optimizing their Sequel II platforms and therefore, be running likely at the higher end of our pull-through metrics. And so that's how I would be thinking about it.

And in some cases, if they want to accelerate, maybe they'd be expanding their infrastructure. Now, interestingly, these are large projects and there's a lot more to the story than just doing the sequencing. It's getting the samples. And the reality is that's a slow process.

And it takes a while for these customers to get the process, get them ready for sampling, and then ultimately get them on the sequencer. And so we would expect them to be scaling up. COVID has not been our friend in this area. But as the world starts to open back up, we would expect them to be ramping up accordingly, and then likely operating at the higher ends of our pull-through metrics to be sure.

Tejas Savant -- *Morgan Stanley -- Analyst*

Got it. And then one on the instrument side. To what extent did some sort of order pushouts you mentioned last quarter come through in the fourth quarter here in the 35 installs? And it looks like you expect instrument revenue momentum to continue in the first quarter here. I'm just trying to parse out how much of that is just more catch up versus sort of strength in the order book and new orders that came in, in 4Q.

Christian Henry -- *President and Chief Executive Officer*

Yes. I think there was definitely some strength in the order book in 4Q. And as I talked about, there were some installations that we couldn't get across the goal line because we couldn't travel. So hopefully, those will get installed in Q1.

But I think the Sequel IIe is a very powerful instrument in the sense that it allows us to reach into customers that don't have the compute infrastructure. And that, coupled with the excitement around COVID surveillance, coupled with the accuracy of HiFi and the precision FDA studies that have been done to show how powerful our system can be on that front, basically or generally increasing demand across the board and getting -- a lot of customers are excited about where we can take this technology. So I think in Q4, the Sequel IIe launch helped us, some of that is carrying over into Q1, and I suspect we'll be a pretty common theme throughout the year.

Tejas Savant -- *Morgan Stanley -- Analyst*

Got it. And one final one for me here on the IIe, actually. Are you starting to see early adopters of the platform perform more long-read sequencing given the time data storage and compute cost savings generated by the enhancements?

Christian Henry -- *President and Chief Executive Officer*

It's a little too early to tell. Usually, when you launch a new system, it takes a quarter to two to really kind of see where the metrics might settle out. And so why don't we try to update everyone on that as we get a little bit deeper into the year here.

Tejas Savant -- *Morgan Stanley -- Analyst*

Got it. Fair enough. Thanks.

Got it. Fair enough. Thanks.

Christian Henry -- *President and Chief Executive Officer*

Yes. Thank you.

Operator

Your next question comes from Tycho Peterson with J.P. Morgan. Your line is now open.

Tycho Peterson -- *J.P. Morgan -- Analyst*

Hey, thanks. I'll add my congrats to Ben as well. It's been great working with you over the years. Christian, I want to go back to the $900 million infusion from SoftBank, and I understand it's early days looking at organic and potentially inorganic investments.

But one of the questions we got today is whether this can help accelerate the timeline to the $1,000 platinum grade genome. You've been kind of marching down this path for a while. To what degree do you think it can help accelerate some of those developments?

Christian Henry -- *President and Chief Executive Officer*

I think it can clearly help because we will be aggressive in investing. I think what it probably does more than maybe it shaves a little bit of time off, but it also helps improve the certainty by which the time goes. And so when you get into these complex development projects, as you can imagine, you're trying to manage to a goal-line to get a product out to market, but you're also trying to make sure you stay focused and get the right product out on time. So although we may be able to bring the timeline in some, it's more likely that what it'll do is help us prevent the timeline from getting pushed out too much, if that makes any sense, Tycho.

Tycho Peterson -- *J.P. Morgan -- Analyst*

It does, yes. And then on Invitae, I know you said no revenues here in the near term. I just want to make sure there's no milestones that could be triggered as part of the program. And then to what degree do you think payors are ready for whole-genome in the clinic? Or are you going to have to do some heavy lifting on that front?

Christian Henry -- *President and Chief Executive Officer*

Yes. That's a good question, Tycho. So with respect to revenue, obviously, Invitae is a customer already. We've talked about the collaboration we're doing with them on the epilepsy project.

So we will have revenue from that side. But with respect to the collaboration, it really is a true partnership where they're going to -- we have a joint steering committee. In fact, our first joint steering committee meeting is, I believe, next week, our first significant. So there's planning and that we're already starting down the development pathway.

And so Invitae will be reimbursing us for that. So we'll see cash flows, but not revenue as kind of Susan outlined. And we'll see that sooner rather than later. And I'm sorry.

I forgot the other part of your question there, Tycho.

Tycho Peterson -- *J.P. Morgan -- Analyst*

Payers or are payers ready for whole-genome sequencing.

Christian Henry -- *President and Chief Executive Officer*

Yes. So I think the question becomes -- the question is all about what's the value of the genome and what's the price. And I believe that we, with Invitae, will be able to price the genomes at a low enough price that it will be competitive with other types of tests out there. So for example, exomes and other types of things.

And if you can continue to demonstrate the increased diagnostic yield, which we're seeing through a number of our collaborations, then it becomes likely that payers are going to be more excited to actually pay for these things. That being said, each payer is going to be -- particularly in the United States, each payer is going to be its own entity, and we're going to have to work with them. And we're going to put -- that's another great reason why we've decided to do partnerships here because the Invitae team has a lot of expertise in that area. And we will build some expertise, but the truth is we want to rely on our partners if that makes sense.

Tycho Peterson -- *J.P. Morgan -- Analyst*

Yes. That's helpful. And then last one on the COVID front. I'm just curious how you're sizing the viral surveillance opportunity? And how much of the variance sequencing do you think ends up being done on short

surveillance opportunity? And how much of the variant sequencing do you think winds up being done on short read versus long read?

Christian Henry -- *President and Chief Executive Officer*

Well, I think the -- we haven't put -- I don't have an answer in terms of absolute sizing at this point. I know there's a lot of funding that's coming into this area through -- we just saw an appropriation of over $1 billion that is trying to get through Congress right now, which I think is only good for us. We're seeing it on a global basis, though. We're seeing in Germany, in the U.K., etc.

But I think that long versus short will really be dependent on how quickly we can get into the market. One thing I would say is that our long-read sequencing capability, the pricing is extremely competitive with short reads, and the information you get is fundamentally better. For example, you get all the phasing information, which allows you to really understand what's going on in a much deeper way. And so we're absolutely price competitive.

The LabCorp protocol that we've talked about, you can multiplex up to 900 samples per run, and so it's just a very compelling value proposition. And it's up to us -- I think the answer will be it's up to us in terms of how fast we can move and get in front of the right people. And we're making a lot of progress there already.

Tycho Peterson -- *J.P. Morgan -- Analyst*

OK. Thank you.

Operator

Your next question comes from Rachel Vatnsdal with Piper Sandler. Your line is now open.

Rachel Vatnsdal -- *Piper Sandler -- Analyst*

Hi. This is Rachel on for Steve. So in the clinical space, you guys have announced a number of impressive partnerships, so with the Asuragen and Children's Mercy and others. What else can we expect to see from PacBio in the partnership segment? And how should we think about the cadence of these new clinical partnerships? And then also, given your new capital influx, will you guys be pursuing clinical applications on your own or you stick with partnerships in the near term?

Christian Henry -- *President and Chief Executive Officer*

Yes. I think strategic -- thank you for the questions. I think we have aggressive internal goals on launching more clinical partnerships. And I would expect them to look similar to what we're doing, for example, with Children's Mercy.

For example, focused in rare and undiagnosed disease as our first real area to continue with our objective to continue proving why a PacBio HiFi genome is so important in the clinic and why that's so useful. And so I would anticipate that we would be trying to put at least -- put several in place this year. And it's a bit aperiodic as each deal takes its own -- life of its own to get them across the goal line. I think one of the things that the capital does is it allows us to think much more creatively about how we get into these partnerships, how big they can become because we have the financial wherewithal to help really drive and build this market out.

With respect to pursuing clinical applications on our own, we're still of the belief that our core competencies are creating the great technology and partnering with others. And so our general preference is to be partnering with others with that core expertise and possibly in certain situations, developing our own clinical product or capability. But we really want to be known as the company that's willing to partner with all of these clinical providers and build our business that way because we think that will make more sense for us over the long term.

Rachel Vatnsdal -- *Piper Sandler -- Analyst*

Great. And going off of that. So as you guys continue to lower the cost, what new markets do you think will be the first to consider shifting to a long-read platform in the clinical space, really like beyond the clinical partnerships that you have, so like rare diseases, for example? And could you talk about the sizes of those opportunities and what you guys need to do to start to capture those markets? And that's all for me. Thanks.

Christian Henry -- *President and Chief Executive Officer*

That's a mouthful, for sure. Mark Van Oene is on the line. Maybe Mark wants to talk a little bit about some of the areas where we think long reads can penetrate. Mark, do you want to try that one? Sorry, we're remote, too.

So it makes it a little trickier.

Mark Van Oene -- *Chief Operating Officer -- Analyst*

Yes. Happy to take that one on for you. So I do think there's a big opportunity still for longer sequencing. And Christian talked about segmenting the portfolio.

And I'm going to just reiterate, there's nothing more important than delivering on this product and the entire workflow for the Invitae collaboration and getting into the clinical whole-genome sequencing opportunity. But I do see a big opportunity for us to deeper penetrate into labs with the Sequel IIe or extensions of that Sequel IIe is the thousands of Tier 2 core labs or the thousands of clinical testing labs that will require the partner and build out the workflows and automation and reporting in ways that we just haven't up until now. So I think expanding our commercial efforts is critical for us to getting into that new segment of lab. So think of that as just lab penetration for long-read sequencing.

There are also a number of extensions of markets that long reads already will benefit. And when I think about clinical applications here, it's differentiation with HLA testing for transplants or pharmacogenomics or No-Amp regions. And so it's not just clinical whole-genome sequencing. I do think there's a big clinical targeted market opportunity for long reads.

I also think we're way underpenetrated in transcriptomes. And so the ISO-Seq type applications to look at full-length isoforms. And look at the isoforms that exist and spring pull those in with either single cell or bulk RNA studies is a great opportunity for us to start to explore, especially if you think about clinical oncology. And then what I always say to people is we just don't know yet what the next applications are going to emerge because not enough people have been using the technology.

And so as we scale our customer base, I expect it to be a series of new applications that are going to emerge for us to take on and commercialize and get to the market.

Rachel Vatnsdal -- *Piper Sandler -- Analyst*

Perfect. Thank you.

Operator

[Operator instructions] We have a question from Kyle Mikson with Cantor Fitzgerald. Your line is now open.

Kyle Mikson -- *Cantor Fitzgerald -- Analyst*

Hi, guys, thanks for taking the questions. And I want to congratulate Ben. It's great work with you for the past -- over the past year or so. And then also congrats on the investment from SoftBank.

And I know it's been asked a bunch of times during the call, but can you just help us think about the uses of cash over the next few years as it relates to this investment, in particular? And I know there's a ton of ways to allocate capital, but in the near term, how are you prioritizing some of those buckets like the sales force and product development, the back end technology, like you mentioned, Chris, then maybe some of the acquisitions? I'm just curious what your kind of perspective and what your thoughts are regarding kind of the prioritization of that you want the inflow of cash? Thanks.

Christian Henry -- *President and Chief Executive Officer*

Sure. And thanks for the question. When you think about prioritization, the first thing we have to do is go back to our core strategies of what are we trying to get accomplished here over the next couple of years. And the first thing where there's low-hanging fruit and direct revenue growth opportunities is scaling our infrastructure on the commercial side.

You heard Mark talk a lot about several different applications where we have a very small presence today, yet we have very powerful technology and capabilities. There are thousands of laboratories out there many of which we just don't even call on. And so I think you'll see us continue to accelerate our -- the money from SoftBank helps us accelerate that opportunity. For example, in Europe, although we were budgeting a significant growth in headcount because we really are underpenetrated there.

Now, we can think bigger about how do we fully build out that team and how do we take advantage of this incredible opportunity with, for example, COVID surveillance sequencing, to build out our capability across the board. So I would say commercial scaling is still going to be front and center. On the R&D front, the ability to take on multiple projects simultaneously is a core competency that we are building. And that requires more infrastructure around the R&D team, not just the R&D people itself.

So it's project management, its strategic planning and so that we will be investing incremental resources to enable us to ensure we can be successful at developing multiple products at the same time. And I think that's core of our technology -- or core to our strategies because if we can get that multiproduct portfolio accelerated and into the market, then we can reach more and more customers and leverage the investments in the sales force, for example, if we can drive the end-to-end workflow, there's opportunities in sample prep

There's opportunities to monetize the informatics but really have -- in order to do that, we have to have highly automated, highly production line capabilities, and we're going to make investments in that to make sure that we can do that. And then lastly, inorganic growth or M&A or partnership, there are real opportunities out there that I think would be highly complementary with the company.

The first thing you have to think through when you start to think about things, those opportunities is, obviously, are they in markets where you can bring something to the table. And then secondly, do you have a management team that can execute and make sure that when you make an investment that you can get the maximum benefit out of it. And we worked really hard over the first part of my tenure here as CEO to build out that management team and capability. And I'm proud to report that we've got a great team, and we're just getting started.

There's a lot more opportunity for us to bring great people on board. So now, we have that in place. And so now it's really thinking strategically looking for people that share the same vision, people and companies and organizations that share the same vision of us that we have and then putting use leveraging the resources that we have to kind of build our business and create scale. So that's a lot to it, but I think it's kind of -- you have to think about it in that order.

Susan Kim -- *Chief Financial Officer*

And, Kyle, this is Susan. I'll just add just a couple of comments with respect to this year. In terms of our organic investment, I had talked a little bit about it during my prepared remarks. But to put it into perspective, in terms of the investments that we're making to drive for long-term growth, we are adding over 100 headcount across the company, whether or not they all come on board, it still remains to be seen, but we are pushing hiring quite a bit, and so you'll see us ramp and our operating expenses will ramp accordingly.

Kyle Mikson -- *Cantor Fitzgerald -- Analyst*

OK. Thanks, guys. I really appreciate that. And I guess just sticking with this theme, I don't keep kind of light.

But Chris, you referenced the $20 billion TAM last month. I just wanted to hear your view if this investment kind of accelerates your ability to penetrate deeper or expand, I guess, in that market? And then you were talking about which markets could be accessible in the near term. But just as it relates to both accelerating the push into those markets, is this tailwind to headwind? Just wanted to hear your thoughts there. I appreciate your comments.

Thanks.

Christian Henry -- *President and Chief Executive Officer*

Yes. No, it's a good question. And the truth is we wouldn't have taken this investment if we didn't think there was opportunities for us to accelerate our potential into these large TAMS. The sequencing market is only getting larger.

We have a clear opportunity to lead at the whole genome level of sequencing. And we have a clear opportunity to create a great business around other aspects of the market like Mark outlined earlier. And so this investment really brings an incredible partner to the table in SoftBank. And their reach and their resources, I think, will help us expand our business straight away.

But then over the long run here, we will be able to take advantage of having this capital to accelerate our opportunity into these TAMs and drive growth. And at the end of the day, my core strategy is how do we drive scale and growth as quickly as possible. We have an incredibly powerful set of technologies already, but what can we do to go even faster. And that's what we're going to be working on.

Kyle Mikson -- *Cantor Fitzgerald -- Analyst*

Got it. All right. That's perfect. I appreciate your answer there.

And I just wanted to talk about Invitae agreement a little bit. It's obviously very promising. Congratulations on it. Of course, will the spending -- you mentioned like $20 million to $25 million in expenses, I guess, in 2021, Susan.

Is that going to be kind of back-half-loaded? I just wanted to understand how to think about that. And then also, I guess the sequencer will be level II Invitae for favorable pricing, of course. But in terms of broader commercial adoption like for other customers, I believe you mentioned that Christian, when could that occur within this five-year kind of timeline? I wasn't quite clear on that. Thanks.

Christian Henry -- *President and Chief Executive Officer*

Yes. Go ahead, Susan, with the dollars. No, go ahead with the dollars, and then we'll go from there.

Yes. Go ahead, Susan, with the doctors may go ahead with the dollars, and then we'll go from there.

Susan Kim -- *Chief Financial Officer*

Yes. So I'll give you an indication, Kyle, of just in terms of how that investment will ramp over time. So as Christian mentioned, we have kicked off. We're ramping in terms of hiring, as well as the expenses associated with the development of the new platform.

We have our joint steering committee kick-off that is happening next week. And so I would think of it as Q1 because we're here in February, Q1 will be lighter. But then, for the most part, the rest of the year will be pretty linear. Q4 is probably slightly more than obviously Q1, just given the nature of ramping a whole new program within the company.

Christian Henry -- *President and Chief Executive Officer*

Yes. And with respect to the products, there is no time associated with, in other words, once we get the product built, the new sequencer built, we'll be able to broadly commercialize it and scale it accordingly. Of course, we're going to give Invitae priority. Any time you develop a new product, as you go through the scale-up, we're going to focus exclusively on Invitae, but that's not because they have an exclusive right.

That's just because they are a partner and collaborator, and we want to ensure that they are absolutely successful, and we're so thrilled to be part of that with them. But we will be able to quickly commercialize that product as we ramp up accordingly.

Kyle Mikson -- *Cantor Fitzgerald -- Analyst*

OK. All right. Thanks. And I know I heard you mention the non-exclusivity.

I guess that's part of it. So just on last like softwall kind of question. So I know you guys have released some -- or I guess total source here really has some of this like pediatric and rare disease data kind of regarding the partnership with Children's Mercy, Kansas City. But when can we see some new diagnostic proof statements coming out in the near term? And I know they're presenting at AGBT.

I was wondering if there could be any update there regarding new data. Thanks.

Christian Henry -- *President and Chief Executive Officer*

Yes. I mean, I think we'll leave that to our collaborators as they -- we don't want to steal their thunder. But the reality is that there's a lot of great work going on. We're on the road to pursuing several new partnerships.

And one of the things you can also see HudsonAlpha just released some data just recently over the last several days or the past week. And so you should check out the HudsonAlpha release because that's a very powerful proof statement.

Kyle Mikson -- *Cantor Fitzgerald -- Analyst*

OK. Congrats on the progress and all the updates, guys. Thank you.

Susan Kim -- *Chief Financial Officer*

Thank you.

Christian Henry -- *President and Chief Executive Officer*

Thank you very much. Thanks for the support.

Operator

There are no further questions at this time. I will now turn the call back to Christian Henry for closing remarks.

Christian Henry -- *President and Chief Executive Officer*

Well, thank you, everyone, for joining us today. And we look forward to speaking with you on our next call. And if you have questions in the future, please feel free to reach out. So thank you very much.

Operator

[Operator signoff]

Duration: 68 minutes

Call participants:

Trevin Rard -- *Investor Relations*

Christian Henry -- *President and Chief Executive Officer*

Susan Kim -- *Chief Financial Officer*

Doug Schenkel -- *Chief Financial Officer*

Tejas Savant -- *Morgan Stanley -- Analyst*

Tycho Peterson -- *J.P. Morgan -- Analyst*

Rachel Vatnsdal -- *Piper Sandler -- Analyst*

Mark Van Oene -- *Chief Operating Officer -- Analyst*

Kyle Mikson -- *Cantor Fitzgerald -- Analyst*

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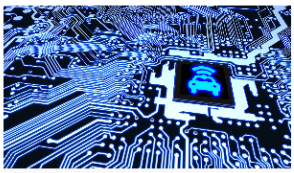

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EXHIBIT D

SMRT® Link release notes (v11.0)

Note: SMRT Link v11.0 is for use with Sequel® II and Sequel IIe systems **only**. Customers running Sequel systems, or those with mixed fleets running Sequel and Sequel II/IIe systems, should continue using SMRT Link v10.2.

SMRT Link server installation

SMRT Link server software is supported on:

  - English-language CentOS 7.x, supported until end-of-life 6/30/2024.
  - English-language Rocky Linux 8.x supported until end-of-life 5/31/2029.
  - Ubuntu 18.04 and 20.04 64-bit Linux® distributions.
  - These supported versions **also** apply to SMRT Link compute nodes.
  - **Note**: PacBio advises **against** new installations of CentOS for use with SMRT Link.
- SMRT Link is **not** guaranteed to work on Linux versions that are no longer supported by the operating systems' vendors.
- SMRT Link server software **cannot** be installed on systems running other versions of UNIX, macOS® or Windows®.
- Several SMRT Link v11.0 features are computationally-intensive and require adherence to the computational and storage requirements listed in the document **SMRT Link software installation guide (v11.0)**.

To install only command-line SMRT® Tools, use the `--smrttools-only` option with the installation command, whether for a new installation or an upgrade. Examples:

```
smrtlink-*.run --rootdir smrtlink --smrttools-only
smrtlink-*.run --rootdir smrtlink --smrttools-only -upgrade
```

Supported chemistry

- SMRT Link v11.0 supports all chemistry versions for Sequel II and Sequel IIe systems.

SMRT Link database note

- SMRT Link v11.0 no longer includes weekly automatic database backups. A database backup is still automatically performed once, during installation or upgrade. Failure to back up the SMRT Link database on a regular schedule risks losing all records in SMRT Link (including users, Data Sets, analyses, barcodes, and references) if a file system or reconfiguration error occurs. The underlying sequencing or analysis files, such as BAM files, are **not** affected. We **strongly** recommend asking your local Linux system administrator to schedule regular weekly backups of the SMRT Link database using standard Linux utilities. For additional details, please contact PacBio Technical Support.

New Features

SMRT Link - SMRT® Analysis

- The term **Continuous Long Reads** is deprecated and replaced by the term **Subreads**.
- SMRT Link analysis applications are now divided into two categories: **Secondary analysis applications**, and **data utilities**.

  - **Secondary analysis applications** produce biologically-meaningful results. These applications accept **only** HiFi reads, and include: Genome Assembly, HiFi Mapping, HiFiViral SARS-CoV-2 Analysis, Iso-Seq® Analysis, Microbial Genome Analysis, Minor Variants Analysis, and Structural Variant Calling.
  - **Data utilities** are used as intermediate steps to producing biologically-meaningful results. All data utilities accept HiFi reads as input, **except** for CCS Analysis which accept only **Subreads** as input.
- The **Microbial Genome Analysis** application replaces the **Microbial Assembly** application in the previous release. The new application also performs base modification detection; this functionality replaces the **Base Modifications Analysis** application in the previous release.
- New data utility to perform **5mC CpG Detection**.
- **HiFiViral SARS-CoV-2 Analysis** now includes a minimum coverage requirement before calling a probability for multiple strains. Samples with less than 70% genome coverage output "NA" instead of a probability.

SMRT Link - Sample Setup

- Can now export calculated values to a CSV file to support lab automation. See **SMRT Link user guide (v11.0)** for details on the fields provided in the CSV export file.

SMRT Link - Run Design

- **CCS analysis output**: In SMRT Link v11.0, the .bam file(s) produced by CCS analysis now contain **only** HiFi reads. A new option allows users to produce .bam files with low-quality reads, similar to how they were delivered in SMRT Link v10.2 and earlier releases.
- Run Designs for Sequel II systems will perform CCS in SMRT Link.

SMRT Link - Run QC

- Run QC now includes an **Instrument Status** view that provides information about PacBio instruments that are connected to SMRT Link.

Known Issues

- **Auto Analysis**: When creating an Auto Analysis job, after completing the **Select Data** step and clicking **Next**, navigating back to the Collections/Samples table may display unexpected columns or data. To resolve this issue, refresh the page and create the Auto Analysis again.
- **Importing Run Designs**: Importing a Run Design CSV file does **not** produce an error when specifying a run that uses three or more Sequencing kit reaction plates. When this occurs, an error displays on the Sequel II or Sequel IIe system after the Run Design is loaded on the instrument. To resolve this issue, edit Run Designs to use **two or fewer** Sequencing kit reaction plates, and reload onto the instrument. Note that the correct error is produced when using the Run Design UI instead of importing a Run Design CSV file.
- **Exporting Run Design**: When exporting a Run Design, Sequencing kit part numbers are numeric, and may be automatically formatted by Microsoft Excel into an exponential number format. Using Microsoft Excel to edit the Run Design export CSV file may then cause failure upon import due to the automatically-formatted Sequencing kit part number. To resolve this issue, reformat the Sequencing Kit column to show **all** digits, turn off the auto-format feature in Microsoft Excel, or use other applications that do not automatically format values in CSV files.
- **SMRT Link Cloud**: Users of SMRT Link Cloud may experience permissions issues with `cromwell`. Contact PacBio Technical Support for workaround instructions.

Fixed Issues

- The display of record numbers shown in Data Management is now consistent with the underlying data and is no longer affected by sorting actions.
- When creating new analyses using the **Copy From** mechanism, users are now given an option to copy from parent analyses.
- Demultiplexing now correctly clips HiFi kinetics tags (`fi`, `fp`, `ri`, `rp`).
- Read Group identifiers assigned during demultiplexing were corrected to address issues with data chunking in some SMRT Link workflows.

EXHIBIT E

← All press releases

APRIL 21, 2022

PacBio and Children's Mercy Kansas City Expand Collaboration Taking a Multi-Omics Approach to Characterize Rare Disease

MENLO PARK, Calif., April 21, 2022 (GLOBE NEWSWIRE) — PacBio (NASDAQ: PACB), a leading provider of high-quality, highly accurate sequencing solutions, today announced an expanded research collaboration with Children's Mercy Kansas City, one of the nation's top pediatric medical systems, to use the multi-omics capabilities of PacBio's Sequel IIe system in the study of genetic disease. The research will apply direct methylation detection and Iso-Seq™ full-length RNA sequencing in their study. A better understanding of the genetic underpinnings of rare disease may ultimately help drive diagnostic yield and potentially enhance care for patients. Children's Mercy is a leader in using PacBio's genomic sequencing technology, approaching 1,000 samples sequenced since 2020.

"Our continued collaboration with Children's Mercy is a great example of PacBio's technology being used at breadth, depth, and scale," said Christian Henry, President and Chief Executive Officer of PacBio. "We believe the Sequel IIe system provides the world's best genomes, and is capable of delivering the most complete methylomes and full-length RNA isoform sequencing. Layering on this rich multi-omics information could potentially yield better insights into the genetic basis of rare disease and provide answers for some families."

Children's Mercy has been using PacBio's HiFi technology for human whole-genome sequencing (WGS) since 2020. Their recent publication in *Genetics in Medicine* (Cohen 2022) describes how HiFi sequencing discovers four times more rare coding structural variants than short-read sequencing, including variants that cause disease. This new collaboration looks to build on that success by studying new methods for the potential detection of rare diseases.

PacBio recently enhanced its Sequel IIe system to detect DNA methylation in human genomes at no additional cost, time, or complexity in library preparation or analysis. Short-read sequencing requires special experiments to detect epigenetic modifications like methylation, and so methylation is often ignored. With PacBio's recent advances, epigenetics is now available in standard runs at no-cost, including for difficult regions of the genome only accessible with long reads.

"We aim to expand sequencing from its interpretation of DNA alone to an integrated test of DNA sequence and its function – in the past we used multiple platforms to achieve the necessary genome characterization," said Tomi Pastinen, MD, PhD, Director, Genomic Medicine Center, Children's Mercy Kansas City. "The systematic application of RNA testing using Iso-Seq and direct methylation detection in HiFi-GS yields information about gene regulation and epigenetic state. We are now working on integrated analyses across hundreds of our unsolved cases and we hope to identify new, previously veiled genomic variants that may be associated with rare disease."

PacBio's Iso-Seq™ method reads full length, end-to-end RNA transcripts, unlike short-read RNA sequencing methods which measure small fragments. Full-length RNA sequencing distinguishes different versions of genes, called isoforms, to capture biology missed by other approaches. Children's Mercy will employ the Iso-Seq method to characterize isoforms that may be associated with disease.

PacBio and Children's Mercy have a long-standing relationship. Last year, Children's Mercy purchased four new Sequel IIe Systems to add to its two existing PacBio systems. These additional systems helped to significantly increase Children's Mercy's large-scale WGS capacity to explore difficult-to-resolve, and hard-to-sequence regions of the genome that are sometimes missed by conventional technologies. With this new collaboration, Children's Mercy will deploy those instruments to look further with multi-omics approaches for methylation and RNA sequencing.

About PacBio

Pacific Biosciences of California, Inc. (NASDAQ: PACB) is empowering life scientists with highly accurate sequencing platforms. The company's innovative instruments are based on Single Molecule, Real-Time (SMRT®) Sequencing technology, which delivers a comprehensive view of genomes, transcriptomes, and epigenomes, enabling access to the full spectrum of genetic variation in any organism. Cited in thousands of peer-reviewed publications, PacBio® sequencing systems are in use by scientists around the world to drive discovery in human biomedical research, plant and animal sciences, and microbiology. For more information, please visit www.pacb.com and follow @PacBio.

PacBio products are provided for Research Use Only. Not for use in diagnostic procedures.

About Children's Mercy Kansas City

Founded in 1897, Children's Mercy is a leading independent children's health organization dedicated to holistic care, translational research, educating caregivers and breakthrough innovation to create a world of

well-being for all children. With not-for-profit hospitals in Missouri and Kansas, and numerous specialty clinics in both states, Children's Mercy provides the highest level of care for children from birth through the age of 21. U.S. News & World Report has repeatedly ranked Children's Mercy as one of "America's Best Children's Hospitals." For the fifth consecutive time in a row, Children's Mercy has achieved Magnet nursing designation, awarded to only about 8% of all hospitals nationally, for excellence in quality care. More than 850 pediatric subspecialists, researchers and faculty across more than 40 subspecialties are actively involved in clinical care, pediatric research and education of the next generation of pediatric subspecialists. Thanks to generous philanthropic and volunteer support, Children's Mercy provides hope, comfort and the prospect of brighter tomorrows to every child who passes through its doors. Visit Children's Mercy and the Children's Mercy Research Institute to learn more, and follow us on Facebook, LinkedIn, Twitter, Instagram and YouTube for the latest news and videos.

Forward-Looking Statements This press release may contain "forward-looking statements" within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and the U.S. Private Securities Litigation Reform Act of 1995, including statements relating to future availability, release dates, uses, accuracy, advantages, quality or performance of, or benefits or expected benefits of using, PacBio products or technologies, the suitability or utility of such products or technologies for particular applications or projects, including in connection with the use of isoform and DNA methylation analyses in rare disease research; the quality of genomes provided by using PacBio's products; the completeness of methylomes and full-length RNA isoform sequencing data created through the use of PacBio products; the potential for rare disease research to yield insights and provide answers for some families; and other future events. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, changes in circumstances and other factors that are, in some cases, beyond PacBio's control and could cause actual results to differ materially from the information expressed or implied by forward-looking statements made in this press release. Factors that could materially affect actual results can be found in PacBio's most recent filings with the Securities and Exchange Commission, including its most recent reports on Forms 8-K, 10-K and 10-Q, and include those listed under the caption "Risk Factors." PacBio undertakes no obligation to revise or update information in this press release to reflect events or circumstances in the future, even if new information becomes available.

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transcriptomes, and epigenomes.

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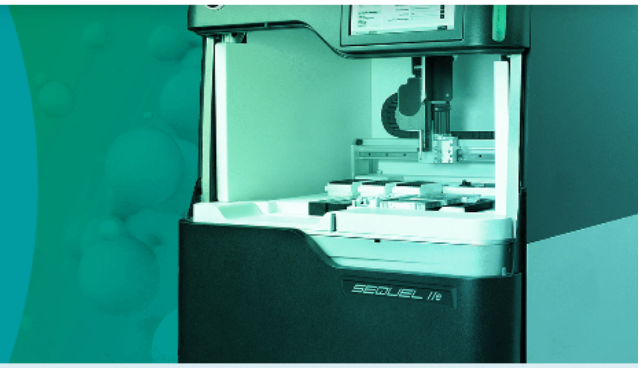
EXHIBIT F

EPIGENETICS

See a new dimension to genomes with the most accurate sequencing reads and DNA methylation in a single experiment

Connect with a PacBio scientist



EPIGENETICS SOLUTIONS

Access the epigenome to explore DNA modifications without any special library preparation needed

HUMAN AND EUKARYOTE EPIGENETICS

Use 5-base HIFI sequencing to study epigenetics of humans and other eukaryotes. Measure 5mC methylation at CpG sites directly from the sequencing instrument without the need for bisulfite treatment or other special library preparation methods.

Download example data

MICROBIAL EPIGENETICS

Build a more comprehensive picture of how microbes use epigenetic modification for immune evasion by characterizing DNA modifications and methyltransferase recognition motifs for 4mC and 6mA.

Learn more

INTRODUCTION TO EPIGENETICS WITH LONG-READ SEQUENCING

The unique chemistry of long-read HiFi sequencing technology enables researchers to directly reveal the epigenetic landscape of samples.

HiFi sequencing provides the most accurate genome-wide calls for SNVs, indels, and SVs. With 5-base HiFi sequencing, the same sequencing library identifies genome-wide methylation patterns associated with gene activity and other biological functions. Further, long HiFi reads enable phasing of the genetic and epigenetic variants into parental haplotypes.

HIFI SEQUENCING

MEASURE THE GENOME AND EPIGENOME

IN A SINGLE SEQUENCING RUN

On-instrument 5-base HiFi sequencing detects 5mC methylation in standard sequencing runs without any changes to library prep or sequencing workflows required.

EPIGENETIC SEQUENCING - HOW PACBIO COMPARES

HiFi sequencing is the only technology that provides accurate genetic and epigenetic information from a single sequencing library.

	Methylation microarrays	Short-read sequencing	Nanopore sequencing	HiFi 5-base sequencing
SNVs	✗	✓	✓	✓
Indels	✗	✓	✗	✓
SVs	✗	✗	✓	✓
Haplotype phasing	✗	✗	✓ Limited	✓
Genome-wide	✗	✓	✓	✓
5mC in CpG contexts	— Limited	— Requires special library preparation	— Requires special data processing. Conflated with basecalling	✓

ADVANTAGES OF EPIGENETIC ANALYSIS WITH 5-BASE HIFI SEQUENCING

With the power of long-read sequencing, you can achieve:

Epigenetics in every run — no bisulfite treatment required

Unlike methods that require chemical conversion of DNA, HiFi sequencing detects modifications in native DNA through impacts on the kinetics of base incorporation.

High accuracy of sequence and methylation

Methylation detection with HiFi sequencing is highly concordant to bisulfite sequencing.

Access the full genome

Access difficult regions of the genome like repeats and centromeres that are beyond the reach of short-read sequencing.

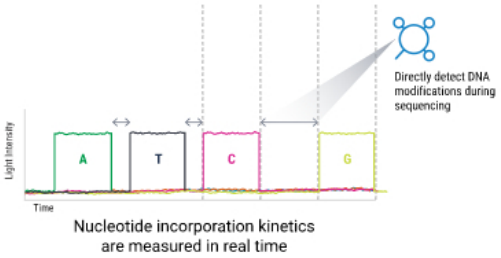
Phasing

Identify allele-specific methylation, whether due to parental imprinting, genetic variation, or repeat expansions.

> ***"SMRT sequencing is opening up new diagnostic avenues, such as the ability to determine tandem repeat lengths, interruptions, and even epigenetics in a single test at base pair resolution."[1]***
>
> – Ardui, et al., 2018[1]

HOW 5-BASE HIFI SEQUENCING CALLS METHYLATION STATUS

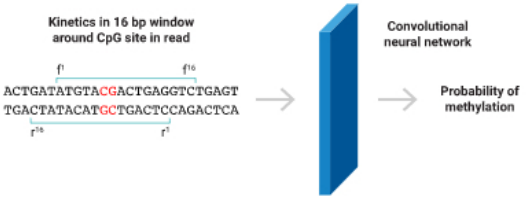
HiFi sequencing provides two channels of information: fluorescence and kinetics. Utilizing both enables highly accurate reads (fluorescence) plus methylation status (kinetics) from a single library.



Nucleotide incorporation kinetics are measured in real time

HiFi sequencing observes a polymerase incorporating fluorescently labeled nucleotides complementary to a native DNA strand. The label identifies the base (A, C, G, T). Epigenetic modifications like 5mC impact polymerase kinetics — how fast bases are incorporated. No special library prep is required.

- A convolutional neural network model processes polymerase kinetics to determine the methylation status of each CpG site in a HiFi read.
- The model runs directly on the Sequel IIe system and is also available in SMRT Link.
- Methylation status is output using the BAM standard MM and ML tags.



APPLICATION BRIEF

MEASURING DNA METHYLATION WITH 5-BASE HIFI SEQUENCING

Genome-wide detection and phasing of genetic and epigenetic variants from a single library prep. HiFi sequencing of a single sample detects methylation patterns across the genome, such as hypomethylation at transcription start sites. Sequencing multiple samples identifies differential methylation.

Learn more

EPIGENETIC ANALYSIS IN ACTION

PB-CPG-TOOLS

The pb-CpG-tools collection provides tools for secondary analysis of CpG methylation data from PacBio HiFi reads. Starting from a pileup of HiFi reads with methylation tags, the tools calculate the percent of reads methylated at every CpG site in the genome.

Access tools

DIRECT DETECTION OF DNA METHYLATION

See how scientists use PacBio sequencing to detect methylation with basepair resolution.

Read publication

GENOME-WIDE DETECTION OF CYTOSINE METHYLATION

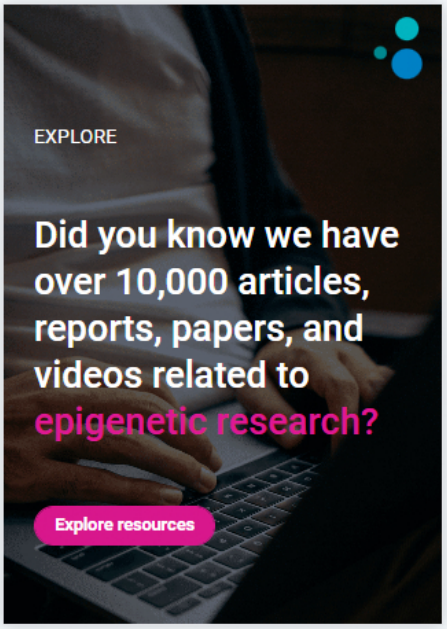
Read how researchers use the kinetics in HiFi reads to determine methylation status at CpG sites.

Access manuscript

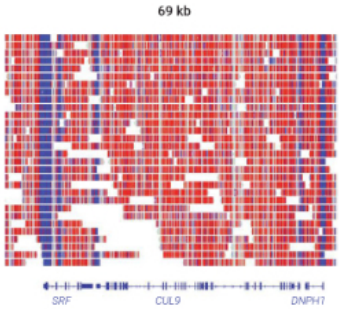
DNA 5MC DETECTION AND METHYLATION PHASING

Read how circular consensus sequencing enables genome-wide detection of cytosine methylation by single molecule real-time sequencing.

Access manuscript



WHAT 5-BASE SEQUENCING REVEALS



REGIONAL METHYLATION PATTERNS

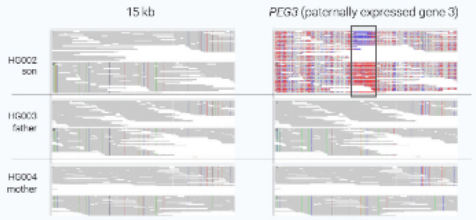
Methylation levels vary across the genome in many species. In vertebrates like human most CpG sites are methylated. Active gene transcription start sites are often hypomethylated.

In this example genomic region, 5-base HiFi sequencing of the human HG002 sample shows overall hypermethylation (red) with hypomethylation (blue) specifically at transcription start sites.

PHASED GENETICS AND EPIGENETICS

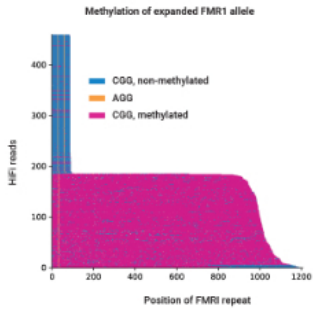
HiFi sequencing enables simultaneous phasing of reads into maternal and paternal haplotypes and detection of methylation. This reveals allele-specific methylation patterns, which can be due to genetic variation (where epigenetic status is affected by a difference in sequence) or parental imprinting (where epigenetic status is affected by whether a chromosome was inherited from the mother or father).

In this example, the HG002/3/4 trio from *Genome in a Bottle*, HiFi reads show the expected maternal imprinting at the gene *PEG3*. HiFi sequencing allows phasing of the haplotypes per sample, the trio identifies which allele is transmitted from which parent, and 5-base sequencing shows allele-specific methylation.



METHYLATION AND DISEASE

Atypical methylation patterns contribute to rare diseases like Prader-Willi syndrome and are important factors in pathogenic repeat expansion, such as the CGG expansion at the *FMR1* locus that cause Fragile X syndrome. With high accuracy, long reads, and methylation detection, HiFi sequencing is ideal for characterizing these repeat expansions.



HiFi sequencing phases and identifies hypermethylation of expanded *FMR1* repeats in NA07537.

APPLICATIONS FOR EPIGENETIC ANALYSIS

5mC at CpG sites is the predominant epigenetic mark in vertebrates like humans. It is also useful — though not comprehensive — in other eukaryotic species such as plants, which employ 5mC methylation in CpG contexts alongside other motifs. For microbes, which employ a wider variety of modifications, alternative analysis tools are recommended.

Methylation	Species	HiFi 5-base sequencing
5mC at CpG sites	Human + other vertebrates	✓
5mC at various motifs	Other eukaryotes, including plants	✓ Useful though partial view
4mC and 6mA	Microbes	Enabled through SMRT Link microbial genome analysis

EPIGENETIC SEQUENCING WORKFLOW AT A GLANCE

STANDARD LIBRARY PREP

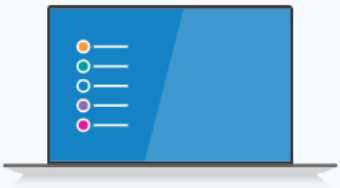
- No bisulfite or other enzymatic treatment

Library prep kits

STANDARD SEQUENCING RUN

- Simultaneously detect accurate base sequence and accurate epigenetic modifications

SMRT sequencing



SIMPLE ANALYSIS

- Detect microbial base modifications and motifs with the microbial genome analysis application in SMRT Link
- Call 5mC at CpG sites directly from the sequencing instrument or in SMRT Link
- Visualize 5mC annotation directly in IGV

COMMON QUESTIONS ABOUT PACBIO EPIGENETIC SEQUENCING

WHICH EPIGENETIC MARKS DOES HIFI SEQUENCING IDENTIFY?

DOES 5-BASE HIFI SEQUENCING DISTINGUISH 5HMC FROM 5MC?

FEATURED LONG-READ SEQUENCING SYSTEMS

5-base genome sequencing is now possible. With PacBio long-read sequencers you can gain immediate access to the epigenome with no special workflow or data processing steps required.

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